Both-faces Hindered Porphyrins. Part 3[1]. Synthesis and Characterization of internally Five-co-ordinated Iron(II) Basket Handle Porphyrins derived from 5,10,15,20-Tetrakis(*o*-aminophenyl)porphyrin

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The synthesis of a series of so-called amide 'hanging base' porphyrins (**10**), (**14**) and (**18**), derived from 5,10,15,20-tetrakis(*o*-aminophenyl)porphyrin (αβαβ-atropisomer) (**3**), in which one of the faces is hindered by an alkylene or an arylene-*p*-bisalkylene bridge and the other face is bridged by a pyridine-3,5-diyl-bisalkylene or an imidazolyl-alkylene chain, is described. The structural assignment of the various compounds is based on the ^{1}H n.m.r. spectra of the free bases, and of their zinc(II) and iron(II) complexes. Unlike the ether 'hanging base' metalloporphyrins, the metallic ion of amide 'hanging base' porphyrins is actually five-co-ordinated by the proximal base. Furthermore, not only is the equilibrium pyridine plane orientation dependent on the length of its linking chain, but the bridging forces the amide protons to point toward the centre of the macrocyle core. These structural properties are potential factors which may affect the binding of dioxygen. The synthesis of a bis-pyridine 'basket handle' porphyrin is also reported.

Chemical systems able to fix molecular oxygen have been extensively reported as active site models of hemoproteins.[2,3] The control of oxygen binding in these substances, as well as in the biological compounds, requires at least the following: (i) the co-ordination of the iron(II) ion by a nitrogenous base on the 'proximal' side; (ii) the steric protection of the heme, in order to protect it from irreversible oxidation into μ-oxo dimers; (iii) the control of the O_2 environment on the 'distal' side.

We reported in the preceding paper of this series,[1] the synthesis of various ether 'hanging base' porphyrins in which the two faces are sterically hindered. In these compounds a pyridine is inserted into one of the two handles to allow five-co-ordination of the central metallic ion, whilst on the opposite side of the macrocycle the second handle forms a cavity for the protection of the oxygen co-ordination site. However, in non-polar solvents, the iron(II) derivatives of these compounds show both a partial intramolecular co-ordination of the base and some intermolecular association. Furthermore, they are poor systems for the stabilization of dioxygen[4,5] as compared with other chemical models recently reported.[6-8] In order to understand the importance of the bridge rigidity and of the presence of polar chemical groups in the cavity between the porphyrin ring and the distal handle for their co-ordination properties, we have synthesized a further series of analogous substituted porphyrins in which the handles are linked to the macrocycle by amido groups. These amide 'hanging base' porphyrins, having a pyridine or an imidazole as axial 'proximal' base, satisfy the three criteria mentioned above and their oxygen adducts have been shown to exhibit remarkable stability.[4,5,9] The latter phenomenon was attributed to the presence of a hydrogen bonding interaction between the oxygen molecule and the amide groups as shown by ^{1}H n.m.r. spectroscopy.[10] These iron(II)–amide 'hanging base' porphyrins when prepared in the absence of exogenous ligand exhibit pure five-co-ordinated spectral characteristics as a result of the greater rigidity of the bridge carrying the proximal base.

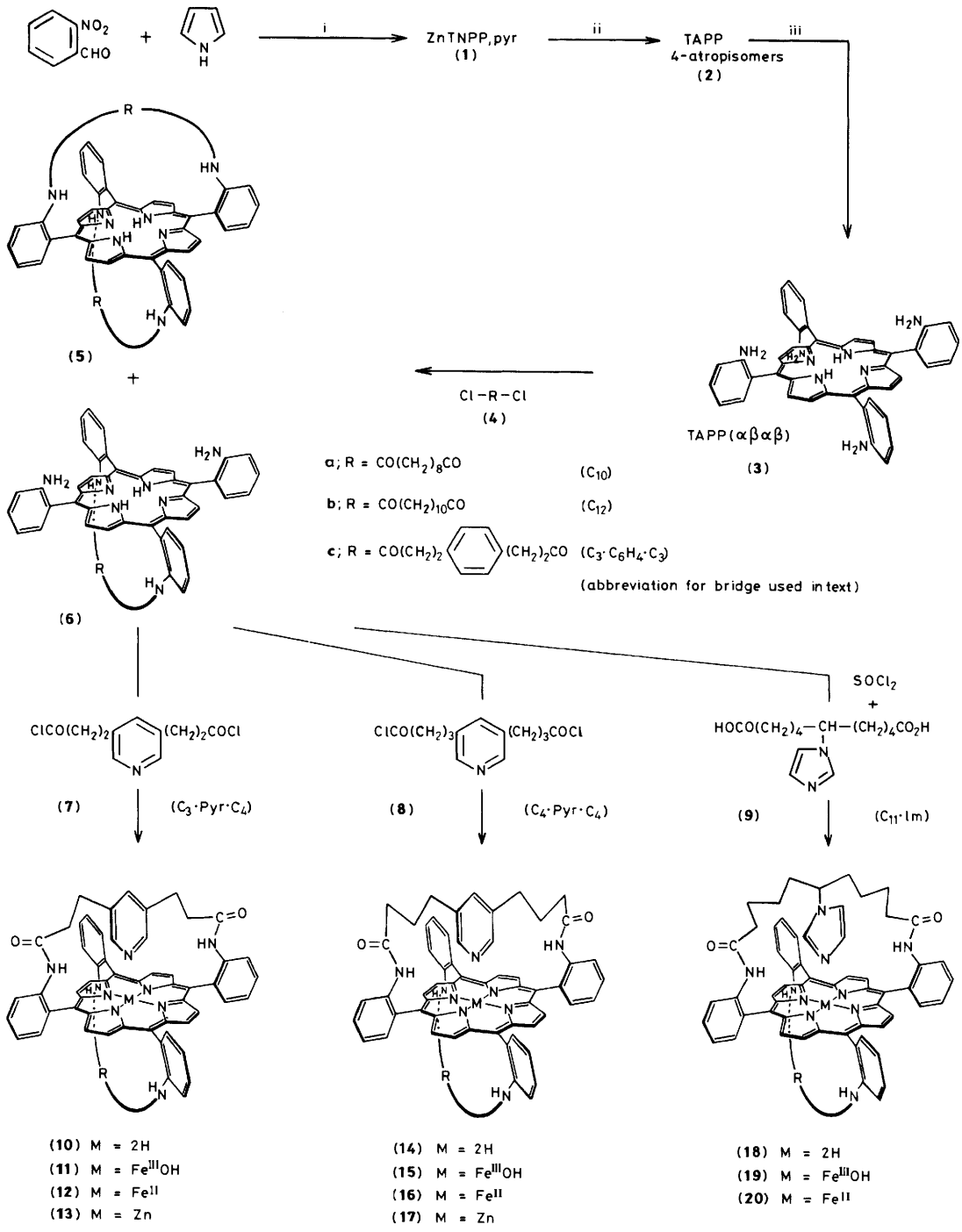
The present paper reports the full synthesis of these new compounds and a bis-pyridine 'basket handle' porphyrin (cross-*trans*-linked isomer). The characterization by ^{1}H n.m.r. spectroscopy of their metallic complexes (Fe^{II}, Zn^{II}) is also presented. The kinetics and the thermodynamics of the oxygen binding for the iron(II) complexes will be analyzed elsewhere.[5]

Results and Discussion

Synthesis of the Amide 'Hanging Base' Porphyrins.—The precursor of the amide 'hanging base' porphyrins (**10**), (**14**), and (**18**) is the αβαβ-atropisomer of the 5,10,15,20-tetrakis(*o*-aminophenyl)porphyrin (TAPP) (**3**). The possibility of using only one atropisomer offered an easy synthesis of the desired cross-*trans*-linked isomer under mild conditions. This eliminated the difficulties encountered in separating the three isomers which were obtained in the preparation of ether 'hanging base' porphyrins.[1] TAPP (**3**) was obtained by a slightly modified version of the procedure described by J. P. Collman *et al.*[11] Thus, direct condensation of *o*-nitrobenzaldehyde and pyrrole, and subsequent reduction of the 5,10,15,20-tetrakis(*o*-nitrophenyl)-porphyrin so obtained gave TAPP contaminated with the parent chlorin. The latter compound cannot be oxidized to porphyrin by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in the usual manner[12] and is extremely difficult to remove.

The solid metalloporphyrin precipitated from the cooled acetic acid solution by condensation of pyrrole with *o*-nitrobenzaldehyde in the presence of an excess of $Zn(OAc)_2 \cdot 2H_2O$. It was soluble enough in organic solvent to be treated with DDQ in a mixture of chloroform–pyridine. Thus, this oxidation afforded pure zinc–porphyrin as its monopyridine complex (**1**) which was isolated in 11% yield after chromatography on silica gel (elution with dichloromethane). Reduction and zinc complex demetallation were simultaneously performed with $SnCl_2 \cdot 2H_2O$ in concentrated hydrochloric acid to afford a mixture of the four atropisomers of TAPP (**2**) with a high degree of purity. The αβαβ-atropisomer porphyrin (**3**) was then isolated by column chromatography (silica gel, 5% ether–dichloromethane).

As for the preparation of ether 'hanging base' porphyrins,[1] amide 'hanging base' porphyrins were synthesized in two steps (see Scheme 1). The first step involved the condensation of (**3**) with one equivalent of the appropriate diacid chloride derivative (**4**) in dry tetrahydrofuran (THF) at room temperature in the presence of triethylamine. The reaction was carried out at high dilution to prevent excessive intermolecular polycondensation and under a nitrogen atmosphere. The diacid chlorides (**4a**—**c**) were obtained by reaction of the corresponding diacid compounds with oxalyl chloride. Different bridging

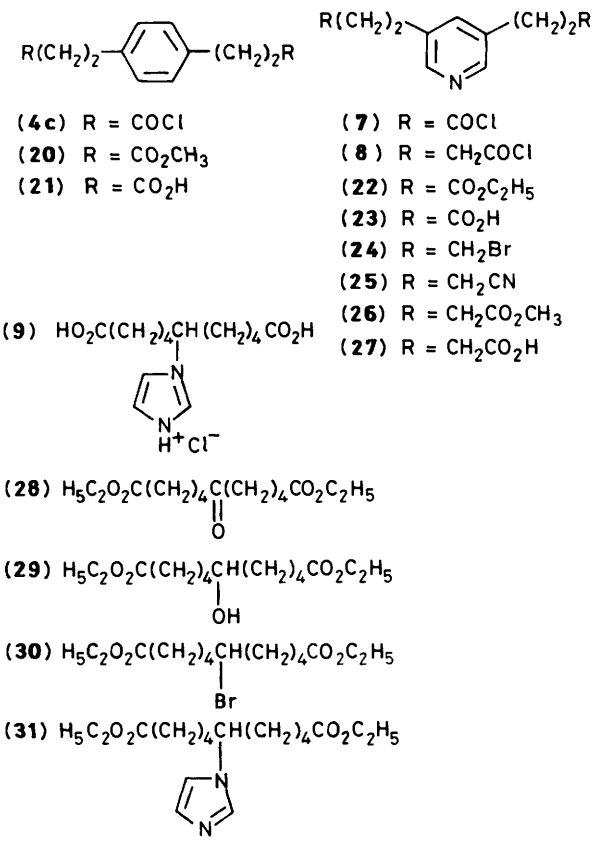


Scheme. *Reagents:* i, $Zn(OAc)_2$, $2H_2O$; ii, $SnCl_2 \cdot 2H_2O$–HCl; iii, chromatography (silica gel, 5% ether–dichloromethane)

groups were used, having either a polymethylene chain, $(CH_2)_n$ ($n = 8$ or 10), or a central phenylene group which is *para*-substituted by two identical polymethylene chains, $(CH_2)_2$. These changes in the length and the nature of the bridges modify the size of the cavity and the environment at the distal site of co-ordination.

Three compounds were observed by analytical t.l.c. of the reaction mixture on silica gel. They were separated by column chromatography on silica gel and identified on the basis of their ^1H n.m.r. spectra. Elution with 1% ether–chloroform gave first some unconsumed starting porphyrin (**3**). Further elution with chloroform–ether (4:1 v/v) gave the most important fraction which was identified as the desired mono-face hindered porphyrin (**6**). The most polar porphyrin eluted with a mixture of chloroform–ether (1:1 v/v) was a both-faces hindered compound (**5**) which corresponds to a cross-*trans*-linked porphyrin in which the bridges bind two opposite *meso*-phenyl groups.[13]

The second step was the coupling reaction of the chain including the pyridine as a proximal ligand. Two different pyridine derivatives were used having a C_n number for the methylene units equal to 2 and 3 respectively in each 3,5-substituted alkyl chain. These two different proximal chains permit the study of constraint and the steric effects of the axial



co-ordination on the physical properties of the iron(II)–amide 'hanging pyridine' porphyrins.[5] As in the first step, the diacid chloride derivatives were prepared immediately before condensation. Pyridine-3,5-bis(propionic acid).HCl (**23**), was treated in dichloromethane–toluene (1:1 v/v) with an excess of thionyl chloride at 50 °C to give the diacid chloride (**7**). 3,5-Bis(3-bromopropyl)pyridine·HBr (**24**) was transformed into the dicyano compound (**25**) which upon subsequent acid hydrolysis yielded the pyridine diacid (**27**); the latter was then treated with pure thionyl chloride to afford the diacid chloride (**8**).

The condensation of (**6**) with the pyridine diacid chlorides (**7**) and (**8**) was carried out in tetrahydrofuran (THF) or dichloromethane following the procedure used in the first step. Treatment of the reaction mixtures in the customary fashion then gave the amide 'hanging pyridine' porphyrins (**10a**—**c**) and (**14**) which were purified by chromatography on silica gel and alumina respectively.

Pyridine was chosen as the axial ligand because of the relative ease of preparing its derivatives. Our interest in the modelling of natural oxygen carrier hemoproteins, however, led us to the synthesis of an analogous compound having imidazole as the axial ligand. Such an amide 'hanging-imidazole' porphyrin could be synthesized by condensing the mono-face hindered porphyrin (**6**) with an *N*-alkylimidazole derivative having two C terminal acid chloride groups.

Diethyl 5-oxononane-1,9-dicarboxylate (**28**), obtained from the corresponding diacid,[14] was transformed, *via* the hydroxy derivative (**29**), to the bromo compound (**30**) in 80% yield. Attempts to purify the latter by distillation, a procedure used successfully with the hydroxy derivative (**29**), led to dehydrobromination to afford the diethyl non-5-ene-1,9-dicarboxylate. Treatment of (**30**) with imidazolyl-lithium in THF under reflux gave diethyl 5-imidazol-1-ylnonane-1,9-dicarboxylate (**31**) in 21.6% yield after silica gel chromatography. Acid hydrolysis of (**31**) afforded 5-imidazol-1-ylnonane-1,9-dicarboxylic acid (**9**).

Several standard diacid chloride-forming reactions failed when they were attempted with (**9**) before the coupling reaction with single-face hindered porphyrin (**6b**). Successful coupling was accomplished only when the diacid chloride was generated *in situ* using $SOCl_2$. Thus, the imidazole derivative (**9**) was treated with 1 equivalent of the porphyrin (**6b**) in dimethylformamide under conditions of high dilution at room temperature, and in the presence of thionyl chloride. The reaction was monitored by analytical silica gel t.l.c. Small quantities of $SOCl_2$ were added as long as the starting porphyrin was present. The expected amide 'hanging imidazole' porphyrin (**18**) was purified by preparative t.l.c. on silica gel plates (20% yield) and isolated as purple crystals (16% yield) after crystallization from dichloromethane–hexane.

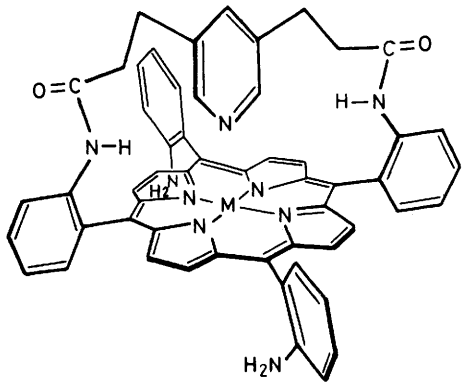
Iron insertion into the amide 'hanging base' porphyrins (**10a**—**c**), (**14**), and (**18**) was performed with anhydrous ferrous chloride in dimethylformamide in the presence of 2,6-dimethylpyridine.[13] The progress of the metal insertion was followed by examining the visible spectrum of the free-base porphyrin. After cooling, acetic acid was added to the reaction mixture under anaerobic conditions. The latter feature is important since the metallo-porphyrin is otherwise highly air sensitive and gives a green compound (as yet unidentified) in high yield (>50%). Nearly quantitative yields of hydroxo-iron(III) complexes were obtained upon work-up of the solutions.

The reduction of haematins into iron(II) porphyrins was carried out using either zinc amalgam in dry toluene or aqueous sodium dithionite, in a two-phase system (toluene–water) under anaerobic conditions. The reduced metalloporphyrins are assigned as high-spin five-co-ordinated species on the basis of their electronic absorption and ^1H n.m.r. spectra (see below).

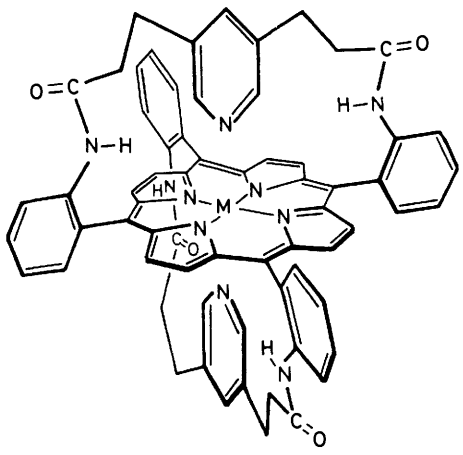
As for the preceding paper[1] we prepared the bispyridine 'basket handle' porphyrin in which both faces were sterically hindered with pyridine bridges. When TAPP (**3**) was condensed with two equivalent of (**7**) in THF, substituted porphyrins and polymeric material were obtained. It was not possible to separate them in their free-base forms. Treatment of the total solid material with an excess of $Zn(OAc)_2 \cdot 2H_2O$ in acetic acid furnished the zinc(II) complexes. After work-up, the products were chromatographed on silica gel. Elution with $CHCl_3$–acetone (1:1 v/v) gave a first fraction which was identified as the single-face hindered porphyrin (**33**). The required compound (**35**) was eluted with $CHCl_3$–MeOH (100:15 v/v) in 7.2% yield. Free-base porphyrins (**34**) and (**36**) were then easily obtained by demetallation of their zinc complexes with aqueous HCl in dichloromethane. Spectrophotometry confirmed the complete formation of porphyrins which were recovered in almost quantitative yield after recrystallization from dichloromethane–hexane.

Iron insertion into the bispyridine compound (**36**) was performed following a similar procedure to that described above. The iron(II) derivative (**38**) was prepared by reduction of iron(III) species (**37**) in dichloromethane using aqueous sodium dithionite. This complex exhibits an electronic absorption spectrum superimposable on the spectrum of dipyridine-hemochrome obtained with unhindered iron(II) 5,10,15,20-tetraphenylporphyrin in the presence of free pyridine (Table 1).

Addition of CO and O_2 to organic solutions of the iron(II)-amide 'hanging base' porphyrins (**12**), (**16**) and (**20**) gave new complexes which were characterized as carbonyl and oxygen adducts respectively on the basis of their absorption spectra (Table 1, Figure 1). A carbonyl derivative was also obtained when (**38**) was exposed to CO. In contrast, there was no modification of its absorption spectrum when dioxygen was bubbled.



(33) M = Zn
(34) M = 2H



(35) M = Zn
(36) M = 2H
(37) M = $Fe^{III}OH$
(38) M = Fe^{II}

Table 1. Absorbance maxima (in nm), and molecular extinction coefficients (in parentheses, in l $mmol^{-1}$ cm^{-1}) of iron and zinc amide 'hanging base' porphyrins complexes, in toluene or dichloromethane.

Amide-[BHP(C_{10})(C_3·Pyr·C_3)]	Fe^{III}–OH^- (**11a**)[a]	422 (83.8)	581 (10.3)	627 (5.9)	
	Fe^{II} (**12a**)[a]	439 (127.2)	535 (8.6)	567 (5.8)	614 (2.9)
	Fe^{II}–CO[a]	426 (223)	545 (10.5)	579 (2.9)	
	Fe^{II}–O_2[a]	425 (99.2)	546 (9.8)	585 (3.1)	
	Zn^{II} (**13a**)[b]	432 (508)	563 (19.1)	605 (6.4)	
Amide-[BHP(C_{12})(C_3·Pyr·C_3)]	Fe^{III}–OH^- (**11b**)[a]	422 (83.6)	580 (9.7)	627 (5.6)	
	Fe^{II} (**12b**)[a]	438 (136)	536 (7.8)	565 (5.3)	615 (2.7)
	Fe^{II}–CO[a]	425 (217.8)	544 (9.6)	578 (2.6)	
	Fe^{II}–O_2[a]	424 (98.3)	545 (9.8)	584 (2.9)	
	Zn^{II} (**13b**)[b]	432 (482.6)	564 (18.3)	604.5 (6.3)	
Amide-[BHP(C_3·C_6H_4·C_3)(C_3·Pyr·C_3)]	Fe^{III}–OH^- (**11c**)[a]	422 (82)	579 (9.9)	626 (5.5)	
	Fe^{II} (**12c**)[a]	439 (124.4)	534 (8.7)	563 (5.8)	614 (2.6)
	Fe^{II}–CO[a]	424 (224.9)	543 (10.8)	576 (2.7)	
	Fe^{II}–O_2[a]	424 (97.7)	548 (10.5)	583 (2.8)	
Amide-[BHP(C_{12})(C_4·Pyr·C_4)]	Fe^{III}–OH^- (**15**)[a]	421 (81)	582 (10.4)	627 (6.1)	
	Fe^{II} (**16**)[a]	437 (138.6)	535 (8.2)	562 (5.9)	614 (2.6)
	Fe^{II}–CO[a]	423 (231.4)	539 (11.2)	574 (2.5)	
	Fe^{II}–O_2[a]	423 (99.8)	542 (10.1)	583 (2.9)	
	Zn^{II} (**17**)[b]	430 (536)	562 (20.7)	601.5 (6)	
Amide-[BHP(C_{12})(C_9·Im)]	Fe^{III}–OH (**19**)[a]	423 (109.3)	544 (9.7)		
	Fe^{II} (**20**)[a]	436 (129.5)	536.5 (10.2)	558 (8.2)	605 (3.7)
	Fe^{II}–CO[a]	424 (214)	541 (11.9)	579 (4)	
	Fe^{II}–O_2	425 (114.4)	546 (12.4)	582 (4.6)	
Amide-[BHP(C_3·Pyr·C_3)$_2$]	Fe^{III}–OH (**37**)[b]	423 (99.3)	537 (8.8)	573.5 (3.3)	
	Fe^{II} (**38**)[b]	426 (156)	534 (16.3)	563 (4)	
	Fe^{II}–CO[b]	424.5 (191.3)	544 (10.4)		
	Zn^{II} (**35**)[b]	434 (445)	566 (17.2)	606 (6.3)	

[a] Toluene. [b] Dichloromethane.

Proton N.m.r.—Proton n.m.r. spectroscopy was used for the characterization of the synthesized compounds. Their spectra are similar to those of the symmetric 'basket handle' porphyrins[13] and of the ether 'hanging base' porphyrins.[1] The symmetry of the pyrrolic protons allowed us to ascertain the obtention of the desired cross-*trans*-linked isomers. In the following, we shall focus attention on the peculiarities of the amide 'hanging base' porphyrins, with regard to the shifts of the amide protons and the co-ordination properties of the pyridine base for the zinc(II) and iron(II) complexes. The proton n.m.r. spectra of the six-co-ordinated iron(II) complexes incorporating CO or O_2 as a sixth ligand have been discussed elsewhere.[5,10]

Free Bases and Zinc Complexes. Typical spectra are shown in Figure 2 for compounds (**10b**) and (**13b**). The most significant feature of these spectra is the large upfield shift of the amide protons arising from the ring current of the porphyrin ring.[15] For the picket fence porphyrin,[16] these protons are shifted by only 7.2 p.p.m. in the same solvent. Thus, the linking chain of

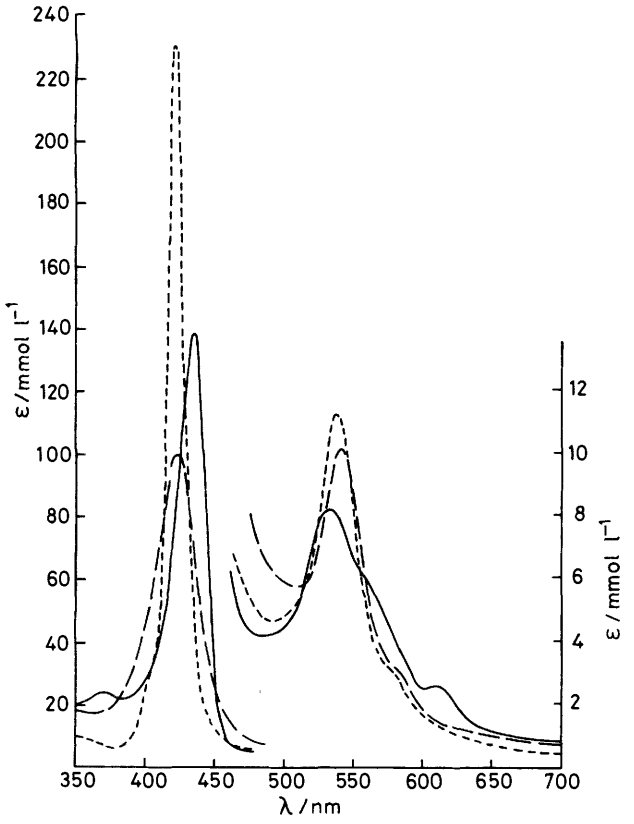


Figure 1. U.v.–visible spectra of the iron(II) complexes of [amide-BHP(C_{12}) (C_4·Pyr·C_4)] (**14**) in toluene at 20 °C. (——) Fe^{II}; (– – –) Fe^{II}–O_2; (- - - -) Fe^{II}–CO

the present models forces these protons to point towards the centre of the porphyrin, with a smaller degree of freedom than in the picket fence model. This property will be important for interpretation of the parameters which govern the binding of the dioxygen molecule to the five-co-ordinated iron(II) complex.[4,10] As a matter of fact, the shift for the amide protons is closely correlated with the tension of the chain (Table 2), the shorter chain leading to the larger upfield shift. The spectra of the unsymmetrical compounds (**10a**—**c**) exhibit two amide proton resonances, each integrating as two protons. One of these appears at a nearly constant field comparable with that observed for (**34**), while the other follows the trend described above with the length of the protecting chain, allowing the specific assignment of these resonances to the two different chains. One exception is for compound (**14**) which incorporates a 'looser' pyridinediyl chain. As a result, the corresponding amide protons are shifted by only 6.64 p.p.m. (Table 2).

Incorporation of zinc into the porphyrin core leads to co-ordination of the pyridine as indicated by the reversal of its proton shifts (Figure 2). In contrast to the ether 'hanging base' porphyrins, the observed ring-current shifts are close to those expected for a five-co-ordinated pyridine-zinc(II) tetraphenyl-porphyrin,[15] suggesting a total co-ordination to the metal.

Also observed is a pronounced lowfield shift of signals for the pyridinediyl chain amide protons upon co-ordination to zinc(II) (Figure 2) for compounds (**13a**—**c**) but not for (**17**) (Table 2). This shift must result from the ring current of the co-ordinated pyridine. It follows that in (**13a**—**c**), the pyridine plane bisects, for most of the time, the N–Zn–N angle during its partial rotation around an axis perpendicular to the porphyrin plane. The mean-plane orientation consistent with the observed C_{2v} effective symmetry is towards the methene bridges to which the pyridinediyl chain is bound. Moreover, this orientation must also be close to the equilibrium position for compound (**13a**—**c**).

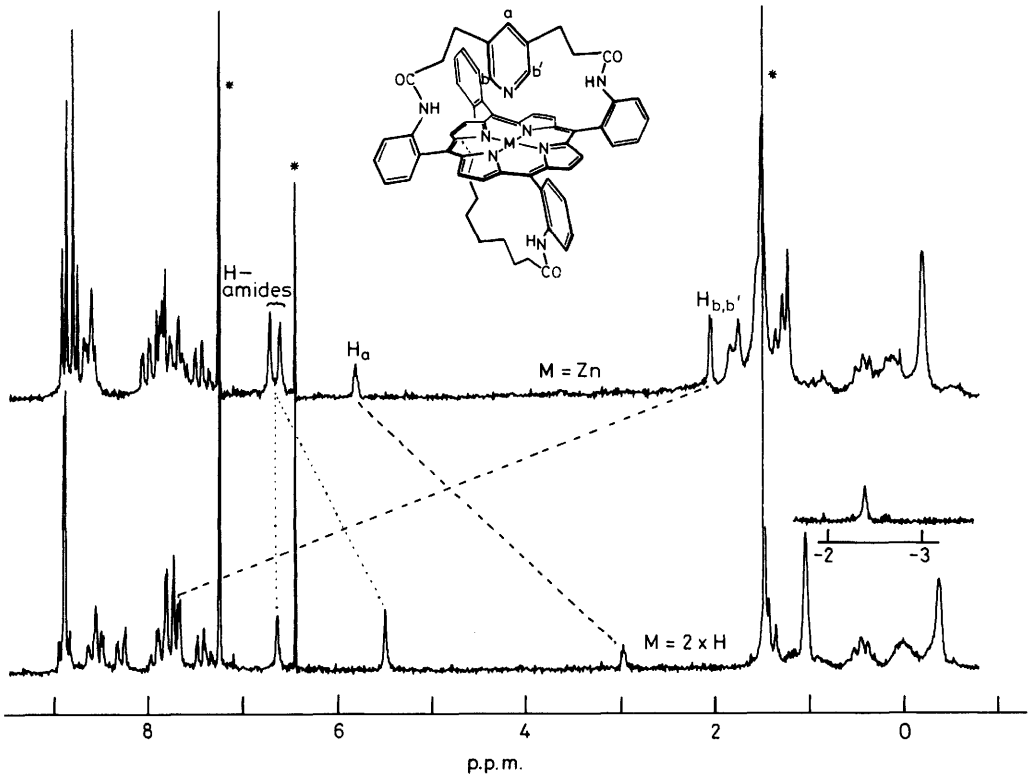


Figure 2. 100 MHz Proton n.m.r. spectra of compound (**10b**) and its zinc complex (**13b**), recorded at 307 K in $CDCl_3$. The asterisks denote solvent impurities

Table 2. Selected proton n.m.r. shifts (in p.p.m.) for the free bases and zinc complexes of the amide 'basket handle' porphyrins recorded in $CDCl_3$ at 307 K. The data for compound (**18**) have been previously published.[9] The numbering is as in Figure 2.

Compounds			*meso*-Phenyl substituents			Pyridine			
	H_{pyr}		NH_2	NH amide		H_a	$H_{b,b'}$	$H_{phenylene}$	NH_{pyr}
(**6a**)	8.93	8.81	3.41	6.34		—	—	—	−2.62
(**6b**)	8.95	8.81	3.46	6.89		—	—	—	−2.63
(**6c**)	8.97	8.84	3.38	5.83		—	—	4.30	−2.48
(**5a**)	8.84		—	6.26		—	—	—	−2.59
(**5b**)	8.84		—	6.77		—	—	—	−2.63
(**5c**)	8.90		—	5.84		—	—	4.47	−2.32
(**10a**)	8.90	8.90	—	6.27	5.53[a]	3.17	7.70	—	−2.36
(**10b**)	8.90	8.87	—	6.66	5.52[a]	3.00	7.67	—	−2.42
(**10c**)	8.95	8.91	—	5.88	5.62[a]	3.37	7.71	4.49	−2.22
(**14**)	8.84	8.80	—	6.64[a]	6.44	4.52	7.30	—	−2.67
(**13a**)	8.89	8.80	—	6.76	6.20	5.84	2.17	—	—
(**13b**)	8.89	8.79	—	6.72	6.63	5.84	2.09	—	—
(**17**)	8.90	8.85	—	6.72	6.41	6.07	1.97	—	—
(**33**)	8.87	8.84	3.2	6.80[a]		5.68	2.17	—	—
(**35**)	8.90		—	6.17[a]		4.58[b]	5.08[b]	—	—
(**34**)	8.96	8.89	*c*		5.63[a]	3.05	7.65	—	−2.47
(**36**)	8.96		—	5.61[a]		3.45	7.72	—	−2.10

[a] Resonances assigned to the amide group of the pyridinediyl chain. [b] The metal is co-ordinated alternatively by one and the other pyridine molecule in an intermediate exchange rate. [c] Resonance not assigned, probably masked by impurities.

Table 3. Proton n.m.r. shifts (in p.p.m. from TMS) for the five-co-ordinated amide 'hanging base' iron(II) porphyrins recorded in a mixture of CD_2Cl_2 and [$^2H_8$]toluene [compounds (**12a**—**c**)] and in pure [$^2H_8$]toluene [compound (**16**)] at 307 K

Compounds		(**13a**)	(**13b**)	(**13c**)	(**17**)	
H_{pyr}		47.9	48.2	47.8	46.9	(T_1 = 41 ms)
		44.2	44.4	44.2	43.2	(T_1 = 43 ms)
$H_{pyridinediyl}$	H_a	17.2	18.7	17.1	21.2	
	$H_{b,b'}$	*a*	≃150	146	143	
	α-CH_2	15.7	16.6	15.3	13.0	
$H_{phenylene}$		—	—	13.2	—	

[a] This resonance cannot be detected above noise owing to the poor solubility of this compound.

In contrast, the equilibrium position must be tilted towards the pyrrolic nitrogen atoms in compound (**17**). In this conformation, the amide protons are located in the region of minimum pyridine ring-current shift, in agreement with the small shift observed for these protons upon co-ordination (Table 2).

Thus, the orientation of the co-ordinated pyridine plane depends on the length of the linking chain. The proton n.m.r. spectra of the corresponding iron(II) complexes described below will give in more detail the reason for this difference.

Iron(II) *complexes.* The proton n.m.r. data for compounds (**12a**—**c**) and (**16**) are collected in Table 3, and the lower trace of Figure 3 presents a typical spectrum obtained at 307 K. Clearly, it exhibits the characteristics of high-spin ($S = 2$) five-co-ordinated iron(II) complexes:[17,18] downfield shifted pyrrolic resonances, negligible pseudo-contact shifts, and a large downfield shift (up to 145 p.p.m.) for the $H_{b,b'}$ pyridine protons. In contrast to the ether 'hanging base' porphyrins,[1] the pyrrolic proton shifts do not exhibit any anomaly in their temperature dependence (Figure 4) and the corresponding Curie plot is practically independent of the nature of the protecting chain. Thus, the electronic ground state of the present iron(II) complexes appears well defined, and the two-states model[1,19] previously proposed for the ether 'hanging base' porphyrins cannot apply. Although the reason for this difference is not clear this does not disprove the above-mentioned model. In fact, it is now known that the microenvironment[20] of such molecules has a pronounced effect on their electronic properties.

For compound (**16**), the libration[21] of the co-ordinated pyridine plane is blocked at low temperatures (Figure 3), and the tilt of the pyridine plane was evidenced by the observation of four pyrrolic resonances. Furthermore, the mean shift now follows a reciprocal temperature dependence close to the Curie law (Figure 4).

In addition to the splitting of the two pyrrolic resonances at low temperature for compound (**16**), a splitting of the resonance assigned to the α-methylene bounded to the pyridine (Figure 3) is observed. This provided us with a qualitative picture of the mechanism of base libration which can be described using Figure 5. This Figure depicts the expected geometry of the chain obtained using a Dreiding molecular model. The conformation of the amide group is chosen such that its proton points toward the porphyrin centre in agreement with its observed shift in the diamagnetic zinc complex. Also, the β-carbon position is such that the steric hindrance of its protons with the rest of the molecule is minimized. This simple model indicates that the length of the four-carbon chains linking the pyridine to the amide nitrogen can be accommodated only by a rotation of the pyridine plane towards the pyrrolic nitrogen atoms. In such a conformation, the two protons α and α′ (Figure 5) are, respectively, in an equatorial and axial conformation relative to the base plane. They are, therefore, magnetically inequivalent, while the two α-methylene groups are equivalent by symmetry, in agreement with the low-temperature spectra. Rotation of the pyridine plane to its symmetrical position requires displacement

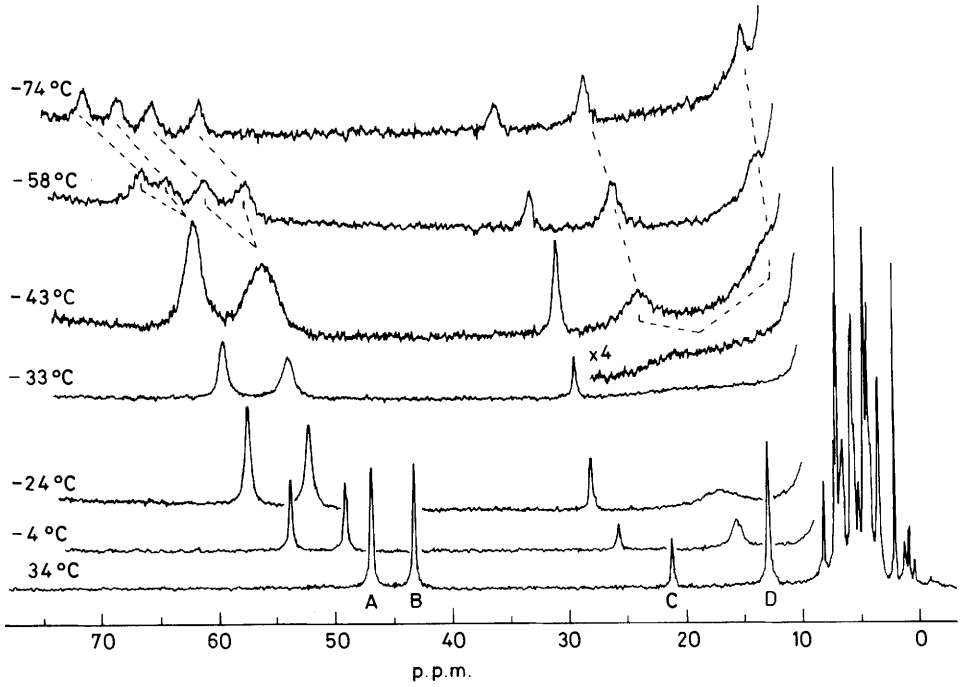


Figure 3. 100 MHz Proton n.m.r. spectrum of compound (**16**) at 307 K (lower trace) and its temperature dependence, recorded in [$^2H_8$]toluene. The pyridine $H_{b,b'}$ resonance at 145 p.p.m. (307 K) is not shown in this figure. The assignment is as follows: A and B, (2 × 4H) pyrrolic protons; C (1 × H), pyridine H_a proton; D (4 H), α-methylene protons bound to the pyridine

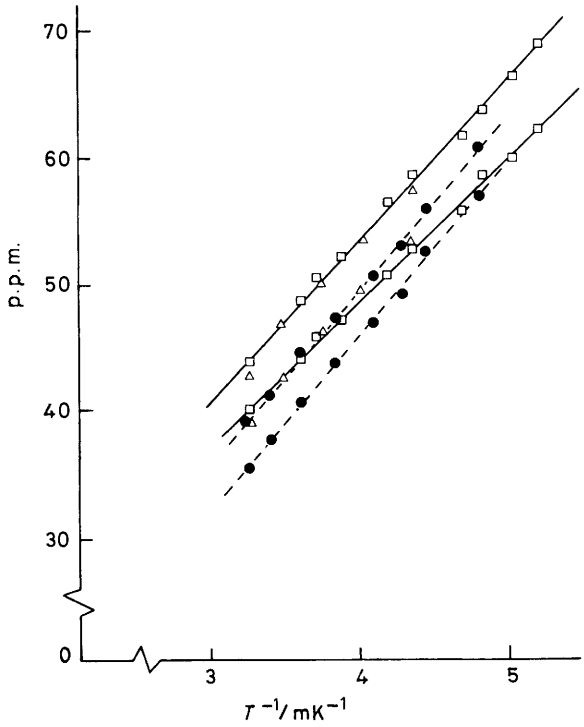


Figure 4. Temperature dependence of the isotropic shifts for the pyrrolic proton resonances: compound (**16**) (■) recorded in [$^2H_8$]toluene, and for the pyrrolic proton resonances: compounds (**12b**) (△) and (**12c**) (●) recorded in CD_2Cl_2

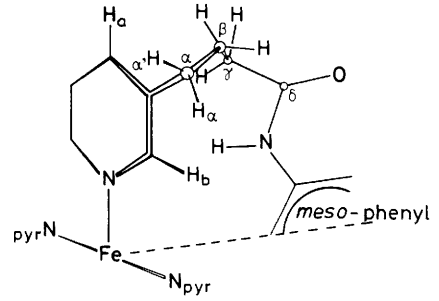


Figure 5. Suggested conformation of the pyridinediyl chain for compound (**16**)

of the β carbon from behind to in front of the pyridine plane. If the pyridine molecule remains co-ordinated during rotation, the close approach of the β-methylene protons with the amide and H_b protons should induce an energy barrier. Indeed, the plot of the exchange rate, as estimated from the observed lineshapes, *versus* the reciprocal temperature gives a small entropy of activation (−2.8 e.u.) and an activation enthalpy as large as 10.7 kcal/mol.

Compounds (**12a—c**) which incorporates a shorter pyridinediyl chain do not exhibit this behaviour, even at the lower temperature of 200 K. A Dreiding molecular model indicates that, although the pyridine plane can undergo libration, its equilibrium position bisects the N–Fe–N angle, consistent with the ring-current effect observed on the amide proton resonances upon co-ordination for the zinc complexes.

This different orientation of the pyridine plane, depending upon the length of the pyridinediyl chain, will have a significant effect on the binding of dioxygen.[5]

Finally, the n.m.r. spectra of the present iron(II) complexes of the amide 'hanging base' porphyrins reveal no trace of association in the temperature range 307—200 K in contrast to the ether 'hanging base' porphyrins;[1] this behaviour is consistent with complete five co-ordination of the central metal.

Conclusions.—The predominant characteristics of the amide 'hanging base' porphyrins can be summarized as follows. First, the bridging forces the amide protons to point toward the macrocycle core, leading to the possibility of direct interaction with the bound dioxygen[4,10] in contrast to the related ether 'hanging base' porphyrins.

Second, the greater rigidity of the amide groups favours the five-co-ordination and eliminates intermolecular associations usually encountered for chelated model compounds.[1,22,23]

Third, subtle proximal effects can be introduced by simply changing the length of the chain which includes the pyridine ring.

Finally, each 'handle' can be modified independently. This allows a comparison of the dioxygen binding properties of a variety of models, differing in (i) the constraints of the proximal base, (ii) the nature of the base, (iii) the chemical and structural nature of the environment of the binding site.

Experimental

All chemicals used were of reagent grade and were purchased from Aldrich. Reaction solvents (Prolabo) for the synthesis were purified before use. Tetrahydrofuran (THF) was allowed to percolate through a dry alumina column and distilled. Dimethylformamide (DMF) was distilled and kept over 4 A molecular seive. 1,2-Dichloroethane was dried over $CaCl_2$. Merck silica gel 60 (40—60 μm) was used for column chromatography. Merck precoated preparative plates (silica gel 60, 2 mm) or (alumina 150, 1.5 mm) were used for t.l.c. Elemental analyses were carried out by the Service Central de Microanalyse du C.N.R.S. Optical spectra in Soret and visible regions were recorded using a Varian DMS 100 spectrophotometer. Proton n.m.r. spectra of free-base porphyrins and their iron(II) complexes in deuteriochloroform and their iron(II) complexes in deuteriochloroform and [$^2H_8$]toluene respectively (C.E.A., France) were measured using a Varian XL 100 spectrometer in the Fourier transform mode using 4 K data points in the frequency domain. Chemicals shifts were referenced to internal tetramethylsilane.

Zinc 5,10,15,20-*Tetrakis*(o-*nitrophenyl*)*porphyrin* (**1**).—A solution of *o*-nitrobenzaldehyde (151 g, 1 mol) and $Zn(OAc)_2 \cdot 2H_2O$ (55 g, 0.25 mol) in acetic acid (3 l) was refluxed. Pyrrole (67 g, 1 mol) was then added and the resulting dark mixture was heated under reflux for 20 min. Chloroform (400 ml) was added to the cooling solution to prevent the separation of tarry by-products. The mixture was then rapidly cooled to 35 °C. The crystalline product was filtered off and washed with chloroform (150 ml) and methanol until the washings were essentially colourless; it was then dried. Analytical t.l.c. on silica gel showed evidence of a green chlorin compound.

The solid was dissolved in chloroform (200 ml) pyridine (15 ml), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone was added. This solution was warmed at 40—50 °C until the adsorption band of chlorin (630 nm) disappeared. The reaction mixture was then placed on a 4 × 25 cm silica-gel column and eluted with dichloromethane. The red eluates were slowly concentrated to give purple crystals (26 g, 11%).

5,10,15,20-*Tetrakis*(o-*aminophenyl*)*porphyrin*(*Mixed Isomers*) (**2**).—Zinc 5,10,15,20-tetrakis(*o*-nitrophenyl)porphyrin (**1**) (19 g, 20 mmol) was dissolved in concentrated hydrochloric acid (800 ml) at room temperature followed by the addition of an excess of $SnCl_2 \cdot 2H_2O$ (65 g). The resulting green mixture was quickly heated to 65—70 °C for 25 min and then neutralized with 20% aqueous ammonia (1 l) until formation of a red-brown suspension. Chloroform (1.4 l) was added to the hot suspension and the mixture was stirred for 1 h. The $CHCl_3$ layer was separated and the aqueous layer was extracted with chloroform (200 ml; × 3). The organic extracts were combined, filtered, and concentrated to 1 l. The resulting solution was washed with dilute aqueous ammonia, water (× 4) and dried (Na_2SO_4). Ethanol (375 ml) and hexane (250 ml) were added, and the solution was slowly evaporated to 500 ml to give a mixture of the four atropisomers (**2**) (9 g, 67%).

αβαβ-5,10,15,20-*Tetrakis*(o-*aminophenyl*)*porphyrin* (*TAPP*) (**3**).—This compound was separated by chromatography on a silica-gel column (5% ether–dichloromethane) as described by previous workers.[11]

Benzene-1,4-*bis*(*propionic acid*) (**21**).—This compound was prepared from dimethyl benzene-1,4-bis(propionate)[24] by saponification; it had m.p. 228 °C (lit.,[25] m.p. 230 °C).

Pyridine-3,5-*bis*(*propionic acid*) *Hydrochloride* (**23**).—This compound was obtained by acid hydrolysis of the corresponding diester (**22**)[1] (yield 76%), m.p. 160 °C (Found: C, 50.85; H, 5.5; Cl, 13.7; N, 5.6. $C_{11}H_{13}NO_4 \cdot HCl$ requires C, 50.9; H, 5.4; Cl, 13.65; N, 5.4); δ (CD_3OD) 8.66 (2 H, s, H *o*-Pyr), 8.52 (1 H, s, H *p*-Pyr), 3.15, 2 × CH_2CH_2Pyr), and 2.8, 2 × CH_2CH_2Pyr).

Pyridine-3,5-*bis*(*butyric acid*) *Hydrochloride* (**27**).—3,5-Bis(3-bromopropyl)pyridine hydrobromide[1] was converted into the dinitrile (**25**) (64%), b.p. 210 °C (2 mmHg). This was treated with hydrogen chloride in methanol to give the dimethyl ester (**26**) (56%). The title compound (70%) was obtained by subsequent acid hydrolysis, m.p. 184—186 °C (Found: C, 54.5; H, 6.5; Cl, 12.4; N, 5.0. $C_{13}H_{17}NO_4 \cdot HCl$ requires C, 54.3; H, 6.3; Cl, 12.3; N, 4.9; δ (CD_3OD) 8.63 (2 H, s, H *o*-Pyr), 8.47 (1 H, s, H *m*-Pyr), 2.93 (t, 2 × CH_2CH_2Pyr), 2.42 (t, 2 × $OCCH_2CH_2$), and 2.0 (br quint, 2 × $OCCH_2CH_2$–CH_2Pyr).

Diethyl 5-*Bromononane*-1,9-*dicarboxylate* (**30**).—The diester (**28**) obtained from the corresponding acid[14] (86%), b.p. 171 °C (2—3 mmHg) was converted into the alcohol (**29**) by sodium borohydride reduction (99%), b.p. 160 °C (1 mmHg). Subsequent bromination with PBr_3 gave the title compound as an oily material (80%) (Found: C, 51.4; H, 7.7; Br, 22.5. $C_{15}H_{27}O_4 \cdot Br$ requires C, 51.3; H, 7.75; Br, 22.75%); δ ($CDCl_3$) 4.14 (q, 2 × CH_3CH_2O), 4.0 (quint, *J* 6.2 Hz, C*H*Br), 2.32br t, 2 × $OCOCH_2CH_2$), 1.67 m, 6 × CH_2), and 1.26 t, 2 × CH_3CH_2O).

Diethyl 5-*Imidazol*-1-*ylnonane*-1,9-*dicarboxylate* (**31**).—n-Butyl-lithium (15% in hexane) (3 ml, 6.4 mmol) was added dropwise to imidazole (880 mg, 12.8 mmol) in dry THF (15 ml) at 0 °C under N_2 and the mixture was stirred for 0.5 h; it was then stirred at room temperature for 15 min. The bromo derivative (**30**) (1.14 g, 3.2 mmol) in dry THF was added and the resulting mixture was heated under reflux overnight. After evaporation of the organic solvent, the residue was taken up in dichloromethane and chromatographed on silica-gel column (3 × 25 cm). The different fractions were detected at 210 nm. Elution with dichloromethane–acetone (3:1 v/v) gave a first fraction which was not identified. The imidazole derivative (**31**) was then eluted with dichloromethane–acetone (1:1) as the second fraction. The solvent was removed by evaporation giving the desired product as a colourless oil (235 mg, 21.5%) (Found: C, 62.4; H, 9.0; N, 8.15. $C_{18}H_{30}N_2O_4$ requires C, 63.8; H, 8.9; N, 8.2); δ ($CDCl_3$) 7.4, 7.05, 6.85 (3 × s, H Im), 4.1 (q, 2 × CH_3CH_2O), 3.89 (quint, *J* 7.3 Hz, CH Im), 2.2 (br t, 2 × $OCOCH_2$), 1.56 (m, 6 × CH_2), and 1.2 (t × CH_3CH_2O).

5-*Imidazol*-1-*ylnonane*-1,9-*dicarboxylic Acid Hydrochloride* (**9**).—A solution of the diester (**31**) (424 mg, 1.26 mmol) in concentrated hydrochloric acid (20 ml) was heated under reflux for 10 h. It was then evaporated and the residue dried *in vacuo* in a desiccator in the presence of potassium hydroxide. The imidazole derivative was immediately used in the preparation of the amide 'hanging-imidazole' porphyrin (**18**) without further purification.

General Procedure for the Preparation of One-face Hindered Porphyrins (**6**).—The appropriate diacid derivative (**4**) (1.5 mmol) was suspended in toluene (10 ml) and treated with oxalyl chloride (4 ml). The mixture was heated at 50—60 °C overnight. Solvent and excess of reagent were removed by evaporation, and the residue was dissolved in dry toluene. The solvent was evaporated and the residual diacid chloride was taken up in dry THF (80 ml). This solution was added dropwise during 2 h to a mixture of 5,10,15,20-tetrakis (*o*-aminophenyl)porphyrin (αβαβ isomer) (**3**) (1.01 g, 1.5 mmol) and triethylamine (420 μl, 3 mmol) in the same solvent (250 ml) at room temperature. Nitrogen was bubbled through the solution during the reaction. After completion of the addition stirring was continued for 2 h. Solvent was removed on a rotary evaporator and the residue was dissolved in chloroform. The solution was washed with water (×3), dried (Na_2SO_4), and concentrated; it was then chromatographed on a silica-gel column (2 × 25 cm). Elution with chloroform–ether (5:0.5 v/v) until the eluate was colourless afforded starting TAPP (**3**). Chloroform–ether (4:1 v/v) was used to elute the mono-face hindered porphyrin (**6**). Finally, elution with chloroform–ether (1:1 v/v) gave a third fraction which was identified by n.m.r. spectroscopy as the cross-*trans*-linked isomer of the 'basket-handle' porphyrin (**5**).[14]

α-5,15-[2,2′-(*Decanediamido*)*diphenyl*]:ββ-10,20-*bis*(o-*aminophenyl*)*porphyrin* (**6a**).—Sebacic acid was used for the preparation of the diacid chloride and (**6a**) was crystallized from dichloromethane–hexane (542 mg, 43%) (Found: C, 74.0; H, 5.9; N, 12.9. $C_{54}H_{48}N_8O_2{\cdot}H_2O$ requires C, 75.5; H, 5.9; N, 13.0). The first fraction was TAPP (151 mg, 15%). The third compound eluted from column chromatography was α-5,15: β-10,20-*Bis*[2,2′-(*decanediamido*)*diphenyl*]*porphyrin* [amide-BHP $(C_{10})_2$] (**5a**). This compound was crystallized from dichloromethane–hexane (256 mg, 17%) (Found: C, 74.9; H, 6.3; N, 10.8. $C_{64}H_{62}N_8O_4{\cdot}H_2O$ requires C, 75.0; H, 6.3; N, 10.9); $\lambda_{max.}$ (ε/mmol l^{-1})(CH_2Cl_2) 421 (280), 514.5 (18), 548 (5.2), 589 (5.6), and 650 nm (3.1).

α-5,15-[2,2′-(*Dodecanediamido*)*diphenyl*]:ββ-10,20-*bis*(o-*aminophenyl*)*porphyrin* (**6b**).—Decane-1,10-dicarboxylic acid was used for the preparation of the diacid chloride. This compound was crystallized from dichloromethane–hexane (638 mg, 49%) (Found: C, 77.2; H, 6.6; N, 12.5. $C_{56}H_{52}N_8O_2$ requires C, 77.4; H, 6.1; N, 12.9). The first fraction was TAPP (140 mg, 14%). The third compound obtained from column chromatography was α-5,15:β-10,20-*bis*[2,2′-(*dodecanediamido*)*diphenyl*]-*porphyrin* [amide-BHP $(C_{12})_2$] (**5b**). It was crystallized from dichloromethane–hexane (330 mg, 20.5%) (Found: C, 76.1; H, 6.7; N, 10.6. $C_{68}H_{70}N_8O_4$ requires C, 76.8; H, 6.6; N, 10.5); $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 419 (279.6), 514 (18.5), 546 (5), 589 (5.7), and 652.5 nm (3.2).

α-5,15-{2,2′-[3,3′-(p-*Phenylene*)*dipropionamido*]*diphenyl*}:ββ-10,20-*bis*(o-*aminophenyl*)*porphyrin* (**6c**).—The diacid chloride was obtained from benzene-1,4-dipropionic acid (**21**). The single-face hindered porphyrin was crystallized from dichloromethane–hexane (500 mg, 38.8%) (Found: C, 75.3; H, 5.5; N, 12.3. $C_{56}H_{44}N_8O_2{\cdot}2H_2O$ requires C, 75.8; H, 5.4; N, 12.5%). TAPP was the first compound obtained from appropriate eluate (80 mg, 8%). The third fraction eluted from column chromatography was α-5,15:β-10,20-*bis*{2,2′-[3,3′-(p-*phenylene*)*dipropionamido*]-*diphenyl*}*porphyrin* [amide-BHP $(C_3{\cdot}C_6H_4{\cdot}C_3)_2$], (**5c**) (Found: C, 73.8; H, 5.6; N, 10.3. $C_{68}H_{54}N_8O_4{,}3H_2O$ requires C, 74.2; H, 5.5; N, 10.2%); $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 420 (277.5), 513 (16.8), 545 (4.2), 586 (5), and 651 nm (3.1).

α-5,15-[2,2′-(*Decanediamido*)*diphenyl*]:β-10,20{2,2′-[(*pyridine*-3,5-*diyl*)[*dipropionamido*]*diphenyl*}*porphyrin* [amide-BHP $(C_{10})(C_3{\cdot}Pyr{\cdot}C_3)$] (**10a**).—A suspension of the diacid pyridine derivative (**23**) (350 mg, 1.35 mmol) in a mixture of dichloromethane (6 ml) and toluene (6 ml) was treated with oxalyl chloride (2 ml). The mixture was heated at 50 °C overnight. The solvent and excess of reagent were evaporated and the residue was dissolved in dry toluene. After evaporation of the solvent to dryness, the diacid chloride (**7**) was dissolved in dry THF (50 ml) and added dropwise to a solution of (**6a**) (520 mg, 0.62 mmol) and triethylamine (600 μl) in the same solvent under a nitrogen atmosphere. After addition, the reaction mixture was stirred for a further 2 h. Water (0.5 ml) was then added to decompose the excess of diacid chloride and the solvent was evaporated to dryness. The porphyrin was taken up in chloroform and the solution washed successively with water (×3) and aqueous hydrogen carbonate, and then dried (Na_2SO_4). After evaporation of the organic solvent, the 'hanging-pyridine' porphyrin (**10a**) was isolated by preparative t.l.c. over silica-gel plates developed with chloroform–acetone (1:1, v/v). Compound (**10a**), which constituted the most important moving band, was crystallized from dichloromethane–hexane (260 mg, 42%) (Found: C, 72.8; H, 5.8; N, 11.2. $C_{65}H_{57}N_9O_4{\cdot}2H_2O$ requires C, 73.4; H, 5.8; N, 11.8%), $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 421 (275.7), 515 (14.8), 549.5 (4.8), 590 (4.8), and 645.5 nm (2.2).

α-5,15-[2,2′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)*dipropionamido*]*diphenyl*}*porphyrin* [amide-BHP$(C_{12})(C_3{\cdot}Pyr{\cdot}C_3)$] (**10b**).—This compound was obtained from single-face hindered porphyrin (**6b**) (868 mg, 1 mmol) and the diacid chloride (**7**) by the foregoing procedure (525 mg, 48%) (Found: C, 74.3; H, 5.9; N, 11.9. $C_{67}H_{61}N_9O_4{\cdot}H_2O$ requires C, 74.9; H, 5.9; N, 11.7) $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 421 (316.5), 515 (17.6), 549 (4.9), 589 (5.4), and 647 nm (2.5).

α-5,15-{2,2′-[3,3′-(p-*phenylene*)*dipropionamido*]*diphenyl*}:β-10,20-{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)*dipropionamido*]*diphenyl*}-*porphyrin* [amide-BHP$(C_3{\cdot}C_6H_4{\cdot}C_3)(C_3{\cdot}Pyr{\cdot}C_3)$] (**10c**)—An analogous reaction to that described above with the single-face hindered porphyrin (**6c**) (441 mg, 0.5 mmol) and the diacid chloride (**7**) gave the desired compound which was crystallized from dichloromethane–hexane (135 mg, 26%) (Found: C, 71.9; H, 5.3; N, 10.7. $C_{67}H_{53}N_9O_4{\cdot}4H_2O$ requires C, 71.8; H, 5.5; N, 11.2) $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 420 (279.7), 514 (15.6), 548 (4.6), 590 (5), and 647 nm (2.4).

α-5,15-[2,2′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{2,2′-[4,4′-(*pyridine*-3,5-*diyl*)*dibutyramido*]*diphenyl*}*porphyrin* [amide-BHP $(C_{12})(C_4{\cdot}Pyr{\cdot}C_4)$] (**14**).—Pyridine-3,5-dibutyric acid hydrochloride (**27**) (170 mg, 0.6 mmol) was converted into the diacid chloride (**8**) by treatment with an excess of $SOCl_2$ (2.5 ml) at 50 °C for 15 min. The excess of $SOCl_2$ was evaporated and the residue was dissolved in dry toluene. The solution was evaporated and dichloroethane (50 ml) was added. The resultant solution was added dropwise during a period of 15 min to a mixture of single-face hindered porphyrin (**6b**) (260 mg, 0.3 mmol) and pyridine (2.5 ml) in the same solvent (150 ml). The reaction mixture was stirred for 1 h at room temperature. The organic solution was washed successively with water (×3) and aqueous hydrogen carbonate and then dried (Na_2SO_4). After evaporation, the residue, in dichloromethane, was chromatographed on a basic alumina column. Elution with dichloromethane–acetone (1:1, v/v) first removed minor fractions. Dichloromethane–methanol (100:5, v/v) used as eluant gave the desired porphyrin which was crystallized in dichloromethane–hexane (200 mg, 50.4%) (Found: C, 74.8; H, 6.0; N, 11.5. $C_{69}H_{65}N_9O_4{\cdot}H_2O$ requires C, 75.2; H, 6.1; N, 11.4); $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 420.5 (303.4), 514.5 (18.1), 547 (4.8), 589 (5.5), and 650 nm (3).

α-5,15-[2,2′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{2,2′-(5-*imidazol*-1-*ylnonane*-1,9-*diamido*)*diphenyl*}*porphyrin* [amide-BHP (C_{12}) (C_9·Im)] (**18**).—5-Imidazol-1-ylnonane-1,9-dicarboxylic acid (**9**) obtained from acid hydrolysis of the corresponding diester (**31**) (see above) (424 mg, 1.26 mmol) was dissolved in dimethylformamide (10 ml) and treated with thionyl chloride (190 μl, 2.6 mmol). This solution was rapidly added to a solution of single-face hindered porphyrin (**6b**) (868 mg, 1 mmol) and pyridine (1 ml) in DMF (100 ml) at room temperature under an atmosphere of argon. The progress of the reaction was monitored by analytical t.l.c. on silica-gel plates (dichloromethane–acetone, 1:1 v/v) and judged complete by the disappearance of the starting porphyrin (R_F 0.65). Two further additions of $SOCl_2$ (190 μl) were necessary. The solution was stirred at room temperature overnight and then evaporated to dryness. The residue was taken up with dichloromethane and water. The mixture was neutralized by addition of aqueous potassium carbonate. The organic layer was separated, washed with water, dried, concentrated, and placed on a 3 × 15 cm silica-gel column. Elution with dichloromethane–acetone (1:1, v/v) gave two minor fractions. A third fraction eluted with 2% methanol–dichloromethane contained the desired imidazole compound. The dichloromethane eluates were evaporated to dryness and the porphyrin was submitted to preparative t.l.c. over silica-gel plates with dichloromethane–methanol (10:2 v/v) development. The amide 'hanging imidazole' porphyrin (**18**), which constitutes the most important moving band, was isolated and crystallized from dichloromethane–hexane (178 mg, 16%) (Found: C, 72.2; H, 6.5; N, 12.1. $C_{70}H_{70}N_{10}O_4$·$2H_2O$ requires C, 73.0; H, 6.5; N, 12.2%); $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 420.5 (300.5), 514.5 (16.8), 548 (4.2), 588 (5.2), and 645 nm (1.6).

Hydroxyiron(III) *Complexes of Amide 'Hanging Base' Porphyrins* (**11**). (**15**), (**19**).—A solution of anhydrous iron(II) chloride (0.5 mmol) in dimethylformamide (5 ml) was added to a stirred solution of free-base porphyrin (0.1 mmol) and 2,6-dimethylpyridine (0.1 ml) in DMF (5 ml) heated at reflux under argon. Insertion of iron was monitored by observation of the disappearance of the absorption band at 650 nm of the free-base porphyrin. After cooling, acetic acid (1 ml) was added. The solution was then evaporated and the resultant residue was dissolved in chloroform. The organic solution was washed with water (× 3), aqueous hydrogen carbonate, and water, and then dried (Na_2SO_4) and evaporated to a small volume. The crude iron(III) complex was chromatographed on preparative alumina plates. Elution with 1% methanol–dichloromethane gave the iron(III)–amide 'hanging pyridine' porphyrin as the major band. A mixture of 2.5% methanol–dichloromethane was necessary to elute the iron(III) complex of amide 'hanging imidazole' porphyrin. A toluene solution of the metalloporphyrin was vigorously shaken with aqueous sodium carbonate to generate the hydroxyiron(III) derivative and then dried (K_2CO_3). Complexes (**11a—c**), (**15**) and (**19**) were precipitated upon addition of hexane.

Iron(II) *Complexes of Amide 'Hanging Base' Porphyrins* (**12**), (**16**), (**20**).—The iron(II) porphyrins were prepared from hydroxyiron(III) complexes in a heterogenous mixture of water (10 ml) containing sodium dithionite and toluene (10 ml) under an atmosphere of argon. After separation of the two phases, the organic layer containing the reduced compound was transferred under inert gas into the optical cell or n.m.r. tube *via* a stainless steel tube. These compounds could also be prepared by reduction of haematins by zinc analgam in dry toluene under argon. Each produces the same iron(II) species as shown by their electronic absorption and ^1H n.m.r. spectra.

Zinc(II) *Complexes of 'Hanging Base' Porphyrins* (**13**), (**17**).—Zinc complexes were synthesized and purified as previously described.[26] Their u.v.–visible characteristics are given in Table 1.

α-5,15:β-10,20-*Bis*{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)*dipropionamido*]*diphenyl*}*porphyrinzinc*(II), [Zn-amide-BHP(C_3·Pyr·C_3)$_2$] (**35**).—Pyridine-3,5-dipropionic acid hydrochloride (**23**) (780 mg, 3 mmol) was converted into the diacid chloride by the same procedure as that used for (**10**). It was added dropwise during a period of 3 h to a mixture of TAPP (**3**) (1.01 g, 1.5 mmol) and triethylamine (6 mmol) in tetrahydrofuran (300 ml) at room temperature under argon. The reaction mixture was stirred overnight and then evaporated to dryness. The residue was dissolved in dichloromethane, and the solution washed with water, dried (Na_2SO_4), and concentrated over reduced pressure.

$Zn(OAc)_2$·$2H_2O$ in acetic acid was added to the porphyrin solution and the mixture was stirred at 50 °C for 5 min. The solvent was evaporated and the crude product was taken up in chloroform; the solution was then successively washed with water, aqueous potassium hydrogen carbonate, and water, and then dried (Na_2SO_4) and evaporated. The residue was chromatographed on a silica-gel (40—60 μm) column equilibrated with $CHCl_3$. Elution with chloroform–acetone (1:1 v/v) gave a first fraction which was identified as the single-hindered porphyrin α-5,15-{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)-*dipropionamido*]*diphenyl*}:β,β-10,20-*bis*(*o-aminophenyl*)*porphyrinzinc*(II) (**33**) (50 mg, 3.6%). A more polar compound was eluted with chloroform–methanol (100:15, v/v). The porphyrin eluates were evaporated, and the residue was crystallized from dichloromethane–hexane to give the desired compound (**35**) (120 mg, 7.2%) (Found: C, 66.6; H, 4.9; N, 11.2. $C_{66}H_{50}N_{10}O_4Zn$·$4H_2O$ requires C, 66.9; H, 4.9; N, 11.8%); $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 434 (422), 566 (17.2), and 606 nm (6.3).

α-5,15:β-10,20-*Bis*{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)*dipropionamido*]*diphenyl*}*porphyrin* [amide-BHP(C_3·Pyr·C_3)$_2$] (**36**).—A solution of (**35**) in chloroform was washed with 0.1M-hydrochloric acid, water, aqueous potassium hydrogen carbonate, and water and then dried (Na_2SO_4). Evaporation to dryness gave the free-base porphyrin (**36**) which recrystallized from dichloromethane–hexane as a purple solid (109 mg, 97%) (Found: C, 70.4; H, 5.3; N, 12.2. $C_{66}H_{52}N_{10}O_4$·$4H_2O$ requires C, 70.7; H, 5.4; N, 12.5%); $\lambda_{max.}$ (ε/mmol l^{-1}) (CH_2Cl_2) 423 (274), 517 (15), 552 (5.2), 590.5 (5.1), and 646.5 nm (2.3).

α-5,15:β-10,20-*Bis*{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)*dipropionamido*]*diphenyl*}*porphyriniron*(III) *Chloride* [Fe^{III}-amide-BHP(C_3·Pyr·C_3)$_2$]OH (**37**).—Incorporation of iron(III) was performed following a similar procedure to that used for the amide 'hanging base. porphyrins (see above). The metalloporphyrin was purified by chromatography on silica-gel plates using dichloromethane–methanol (100:20, v/v) as eluant. Evaporation of the appropriate extraction solvent gave a residue which was washed with aqueous potassium carbonate. Crystallization from dichloromethane–hexane gave the hydroxyiron(III) derivative (**37**).

α-5.15:β-10,20-*Bis*{2,2′-[3,3′-(*pyridine*-3,5-*diyl*)*dipropionamido*]*diphenyl*}*porphyriniron*(II) [Fe^{II}-amide-BHP (C_3·Pyr·C_3)$_2$] (**38**).—This compound was obtained by the reduction of the haematin (**37**) in toluene using sodium dithionite.

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References

1 M. Momenteau, J. Mispelter, B. Loock, and J. M. Lhoste, *J. Chem. Soc. Perkin Trans 1*, 1985, 61.
2 J. P. Collman, *Acc. Chem. Res.*, 1977, **10**, 265.
3 T. G. Traylor, and P. S. Traylor, *Ann. Rev. Biophys. Bioeng.*, 1982, **11**, 105.
4 M. Momenteau, and D. Lavalette, *J. Chem. Soc., Chem. Commun.*, 1982, 341.
5 D. Lavalette, C. Tétreau, J. Mispelter, M. Momenteau, and J. M. Lhoste, *Eur J. Biochem*, in the press.
6 J. P. Collman, J. I. Brauman, T. J. Collins, B. Iverson, and J. L. Sessler, *J. Am. Chem. Soc.*, 1981, **103**, 2450.
7 T. G. Traylor, M. J. Mitchell, S. Tsuchiya, D. H. Campbell, D. V. Stynes, and N. Koga, *J. Am. Chem. Soc.*, 1981, **103**, 5234.
8 B. Ward, C. B. Wang, and C. K. Chang, *J. Am. Chem. Soc.*, 1981, **103**, 5236.
9 M. Momenteau, B. Loock, D. Lavalette, C. Tétreau, and J. Mispelter, *J. Chem. Soc., Chem. Commun.*, 1983, 962.
10 J. Mispelter, M. Momenteau, D. Lavalette, and J. M. Lhoste, *J. Am. Chem. Soc.*, 1983, **105**, 5165.
11 J. P. Collman, R. R. Gagne, C. A. Reed, T. R. Halbert, G. Lang, and N. T. Robinson, *J. Am. Chem. Soc.*, 1975, **97**, 1427.
12 G. H. Barnett, M. F. Hudson, and K. M. Smith, *Tetrahedron Lett.*, 1973, 2887.
13 M. Momenteau, J. Mispelter, B. Loock, and E. Bisagni, *J. Chem. Soc., Perkin Trans 1*, 1983, 189.
14 N. Rabjohn, *Organic Synth.*, Coll. vol. 4, 1963, 555.
15 R. J. Abraham, G. R. Bedford, D. McNeillie, and B. Wright, *Org. Magn. Reson.*, 1980, **14**, 418.
16 J. P. Collman, R. R. Gagne, C. A. Reed, T. R. Halbert, G. Lang, and N. T. Robinson, *J. Am. Chem. Soc.*, 1975, **97**, 1427.
17 H. Goff, and G. N. La Mar, *J. Am. Chem. Soc.*, 1977, **99**, 6599.
18 J. Mispelter, M. Momenteau, and J. M. Lhoste, *Chem. Phys. Lett.*, 1978, **57**, 405.
19 J. Mispelter, M. Momenteau, and J. M. Lhoste, *Biochimie*, 1981, **63**, 911.
20 D. Lexa, M. Momenteau, P. Rentien, G. Rytz, J. M. Savéant, and F. Xu, *J. Am. Chem. Soc.*, 1984, **106**, 4755.
21 L. Latos-Grazynski, *Biochimie*, 1983, **65**, 143.
22 J. P. Collman, J. I. Brauman, K. M. Doxsee, T. R. Halbert, E. Bunnenberg, R. E. Linder, G. N. La Mar, J. Del Gaudio, G. Lang, and K. Spartalian, *J. Am. Chem. Soc.*, 1980, **102**, 4182.
23 M. Momenteau, M. Rougée, and B. Loock, *Eur. J. Biochem.*, 1976, **71**, 63.
24 L. Ruzicka, J. B. Buijs, and M. Stoll, *Helv. Chim. Acta*, 1932, **15**, 1220.
25 A. G. Giumanini, A. Drusiani, and L. Plessi, *J. Org. Chem.*, 1975, **40**, 1844.
26 A. D. Adler, F. R. Longo, F. Kampas, and J. Kim, *J. Inorg. Nucl. Chem.*, 1970, **32**, 2445.

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